Not Just for Workers

Maternal Exposure to Ambient Benzene Linked to Spina Bifida in Infants

Occupational exposure to hazardous air pollutants such as benzene has been linked in some studies to neural tube defects (NTDs), yet to date no one had studied whether exposure to ambient levels of benzene may similarly lead to adverse outcomes. A new study now reveals a positive association between exposure to ambient benzene in outdoor air and increased prevalence of spina bifida [***EHP* 119(3):397–402; Lupo et al.**].

NTDs are a common type of birth defect. They arise when the neural tube fails to close during fetal development, leading to spina bifida (incomplete spinal column formation) or anencephaly (incomplete brain and skull formation). Both genetic and environmental factors, particularly inadequate folic acid intake, appear to play a role in NTDs.

The Texas Birth Defects Registry provided data from 1 January 1999 to 31 December 2004 on 1,108 newborn infants, stillborn infants, and electively terminated fetuses with NTDs. A random set of 4,132 unaffected infants born during the same period served as a control group. Ambient air levels of benzene, toluene, ethylbenzene, and xylene were estimated at the census-tract level using the U.S. Environmental Protection Agency's 1999 Assessment System for Population Exposure Nationwide (ASPEN) paired with mothers' residential addresses at the time they gave birth. After exclusions for missing data and known chromosomal abnormalities or syndromes, 533 spina bifida cases, 303 anencephaly cases, and 3,695 control cases remained for analysis.

Mothers with the highest estimated benzene exposure (≥3 μg/m^3 in ambient air) were 2.3 times as likely as mothers in the reference group to bear children with spina bifida. The relationship between benzene exposure and spina bifida was statistically significant for most levels of exposure above the reference value, but the dose–response relationship was not monotonic (that is, the odds of risk did not increase consistently with each increase in exposure level). Associations between other solvents and spina bifida and between individual solvents and anencephaly also were observed but were not statistically significant.

The study has several potential limitations including possible exposure misclassification, the availability of pollutant data for only 1 year of the study period, and limited information on potential confounders, such as maternal folic acid intake. However, these limitations are at least partially offset by ASPEN's high-quality exposure estimates, the likelihood that pollutant levels were stable during the study years, and mandatory folic acid fortification of foods.

This study is the first to suggest spina bifida prevalence is associated with maternal exposure to ambient air benzene levels. Further study of exposure, genotypes, and maternal nutrient status are needed to confirm this finding.

Julia R. Barrett, MS, ELS, a Madison, WI–based science writer and editor, has written for *EHP* since 1996. She is a member of the National Association of Science Writers and the Board of Editors in the Life Sciences.

A Whale Tale

Using Blubber Biopsies to Characterize Pacific Ocean Pollutant Trends

Expression of the enzyme CYP1A1 in the skin of marine mammals has been shown by multiple studies to indicate exposure to organic pollutants in a dose-dependent manner. A new large-scale monitoring study investigated whether analysis of dermal CYP1A1 expression and organic pollutants in sperm whales (*Physeter macrocephalus*) could reveal oceanwide geographical trends in chemical exposure [***EHP* 119(3):337–343; Godard-Codding et al**]. This is the first known study to assess broad geographic trends in CYP1A1 expression, stable carbon and nitrogen isotopes, and organic pollutant burdens in a threatened whale species.

The authors used immunochemistry to analyze CYP1A1 expression in skin and blubber samples collected from 234 sperm whales from five Pacific Ocean regions. Variation in the whales' trophic level (position in the food chain) was examined by using mass spectrometry to measure nitrogen isotopes in skin samples; enrichment of an animal's tissue nitrogen is known to occur as the animal eats higher on the food chain. The general latitude frequented by the whales—a reflection of where the whales were likely to have been exposed to pollution—was determined by analyzing carbon isotope ratios.

The whales exhibited significant regional differences in CYP1A1 expression. Expression was highest among whales from the Galapagos Islands, a United Nations World Heritage marine reserve, and lowest among whales from sites farthest away from continents. Differences in the whales' age, sex, and diet did not appear to explain regional differences but could not be ruled out unequivocally.

This study did not show a significant correlation between CYP1A1 expression in skin cells and actual pollutant burden in blubber, as measured by analyzing eight sex-specific pooled samples for burdens of polycyclic aromatic hydrocarbons, hexachlorobenzene, polychlorinated biphenyls, and the pesticide DDT, then comparing them with CYP1A1 immunohistochemistry scores estimated for the pooled samples.

However, the small size of the individual biopsies allowed under standards for humane biopsying of marine mammals prevented detailed chemical analyses and limited the power to detect significant associations. Also, the biopsies were limited to the outer blubber layer, which is less metabolically active than deeper tissue. Studies in bottlenose dolphins have shown that CYP1A1 expression in the skin is more strongly related to pollutants measured in deeper blubber than in blubber closer to the skin surface; whether such stratification happens in other cetaceans requires further study.

The study succeeded at identifying regional differences in CYP1A1 expression, providing a baseline for this known biomarker of exposure to organic pollutants. Future studies that profile CYP1A1 expression in cetacean skin biopsies oceanwide are warranted to explore the global distribution of biochemically relevant levels of these chemicals.

Angela Spivey writes from North Carolina about science, medicine, and higher education. She has written for *EHP* since 2001 and is a member of the National Association of Science Writers.

Carnivorous sperm whales are at the top of their food chain.

Vicki Beaver/Ocean Alliance